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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/084,639 | 02/25/2002 | Gregory S. Hageman | 020618-000920US | 6293 |

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| EXAMINER | |
|---|---|
| SAUNDERS, DAVID A | |
| **ART UNIT** | **PAPER NUMBER** |
| 1644 | |

DATE MAILED: 07/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 08/4,639 | HAGEMAN et al |
| **Examiner** | **Group Art Unit** |
| SAUNDERS | 1644 |

*—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

**Status**

☑ Responsive to communication(s) filed on 5/7/04.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

**Disposition of Claims**

☑ Claim(s) 1-9, 13-15, 20-23 is/are pending in the application.

Of the above claim(s)_____ is/are withdrawn from consideration.

☐ Claim(s)_____ is/are allowed.

☑ Claim(s) 1-9, 13-15, 20-23 is/are rejected.

☐ Claim(s)_____ is/are objected to.

☐ Claim(s)_____ are subject to restriction or election requirement.

**Application Papers**

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on_____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on_____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119 (a)-(d)**

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number)_____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received:_____.

**Attachment(s)**

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). 8/12 038 3/29/04 ☐ Interview Summary, PTO-413

☑ Notice of Reference(s) Cited, PTO-892 ☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948 ☐ Other_____

**Office Action Summary**

The amendment of 5/7/04 has been entered. Claims 1-9, 13-15 and 20-23 are pending.

Applicant's election without traverse of Group I (claims 1-9, 13-15 and 20-23) in the reply filed on 5/7/04 is acknowledged.

It is noted that applicant has elected fibulin-6 as the species of macular degeneration associated molecule; claims 1-9 and 14-15 read there upon. All claims of Group I will be examined for 112 issues; also, to the extent that art may be found, all claims will be examined over the prior art.

Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 9, line 3 "the serum sample" lacks antecedent basis.

Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 2 recites new matter.

In claim 2 the Markush group member "fibulin-6" lacks original disclosure support; this has been recited nowhere in the disclosure.

Also the members "type IV collagen, elastin, c-reactive protein, clusterin," and "metalloelastase" appear to have been recited in the para. spanning pages 19-20; what is disclosed therein relates merely to "Drusen-associated phenotypic

or genotypic markers," without any teaching that these "markers" serve as autoantigens. Entry of these members is thus new matter.

Claims 1-9, 14-15, 20-21 and 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant has not adequately described the genus of "macular degeneration associated molecules."

Applicant's teachings regarding what proteins may constitute "macular degeneration associated molecules" (para. Spanning pages 10-11; page 12, first full para; para spanning pages 14-15; page 16, first para; page 31, second full para.) merely set forth a laundry list of various molecules known to exist in macular tissues and/or found in drusen. This listing however does not describe which of those molecules serve as cognate autoantigens of the autoantibodies associtated with age-related macular degeneration (AMD). It is noted that the term "macular degeneration associated molecule" of claim 1 must include retina-associated proteins" of dependent claim 20; again, for this subgenus of "retina associated proteins" there is an inadequate description of which of the many such proteins are those which serve as cognate autoantigens of autoantibodies associated with AMD.

Further, it is noted that claim 2 recites a Markush group of specific molecules; however, the members "type IV collagen, elastin, c-reactive protein,

clusterin, metaloelastase" were disclosed (pages 19-20) as phenotypic or genotypic markers, not as autoantigens.

Claims 14 and 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The genus of "macular degeneration genetics markers," "drusen-associated genotypic markers," and "genetic markers associated with age related macular degeneration" has not been adequately described.

The markers discussed in at pages 18-20 merely set forth a vast list of genetic markers which could be tested; however, this disclosure does not set forth what genetic markers are those associated with AMD, other than those set forth in the para. spanning pages 19-20.

Further it appears that applicant contemplates that this term encompasses "mutant genes which have not been identified" (page 21, first full para). Since applicant therein admits that the mutant genes for AMD have not been identified, applicant's description is that of something unknown and yet to be found in the future by others. This constitutes no description at all. Univ. of Rochester 68 USPQ 2d 1425.

Claims 1-9, 13-15, 20-21 and 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a

way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The instant claims lack enablement for the diagnosis of AMD.

Since the genus of "macular degeneration associated molecules" and the subgenus of "retina associated proteins" have not been adequately described, the method using these molecules as autoantigens has not been enabled. See Univ. of Rochester 68 USPQ 2d 1425, at pages 1434+.

Furthermore the claims are specifically directed to diagnosing AMD, rather than any macular degeneration related disorder; it appears that claims 2 and 13 recite numerous Markush group members which are not autoantigens in the case of AMD. The only listed members that have been disclosed as associated with AMD are fibulin-3 and vitronectin. See page 24 last para; page 30 line 1. Numerous other proteins appear to be autoantigens of other disorders—e.g. for ML; see page 24 last para.

Claims 14 and 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 4 and 23 lack enablement because the genetic markers (mutant genes) for AMD have not yet been identified (page 21, first full para.).

Applicant's claims are thus an invitation for one to conduct undue experimentation to find out something that has been yet undiscovered. See University of Rochester 68 USPQ 2d 1425, at pages 1434+.

Prior to examination over the prior art of record, it is to be noted that the instant claims are given only the benefit of the instant filing date. Parent application 09/845,745 (pre-grant publication 2003/0017501 A1) teaches diagnosis of macular degeneration disorders, including age-related, at para. [0098]+ (according to para. numbering in the pre-grant publication). The examiner notes a mention of immune complexes at [0103]; however, there is no teaching that these contain "at least one macular degeneration associated molecule" as required by instant claim 1.

Furthermore, even if benefit of the 09/845,745 were granted for claim 1, it is to be noted that claim 2 would not have such benefit, since the Markush group of claim 2 recites numerous macular degeneration molecules not disclosed in para [0100]. Likewise instant claims 13 and 20 recite Markush group members not disclosed in para [0100].

No claim is granted benefit of the filing date of grand parent 09/510,230; this shows numerous embodiments, among which the instant invention cannot be found.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-7, 13, 15 and 20-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Hageman (WO 95/17673).

Hageman teaches diagnosis of early AMD by detecting the "presence of autoantibodies to vitronectin in the bloodstream" (page 4, lines 12-13). See also page 26, line 37-page 27, line 5; page 42, lines 18-19; page 42, line 30-page 43, line 12. This anticipates instant claims 1-3, 6, 13 and 20-22.

Regarding claim 5, note teachings of a comparison against sera from normal donors ( page 43, line 3).

For claim 15, note page 26, lines 19-31.

Regarding claim 7, note that any western blotting method inherently involves formation of an unlabelled immune complex (between antigen and analyte autoantibody) on a solid phase (e.g. nitrocellulose), followed by detection with labeled reagents (e.g. labeled secondary antibody labeled biotin-avidin reagents). Formation of immune complexes on a solid phase is deemed encompassed by "precipitation. Note applicant teaches (page 15, last para.) solid phase capture of immune complexes with protein A/G and then teaches "the immunoprecipitates are washed."

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been

obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3 and 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hageman in view of Schuurs et al (3,645,090).

Hageman was cited supra against claim 1. Hageman teaches competitive binding assays. Schuurs et al teach how to perform a competitive binding assay that employs cognate antigen on a solid phase and a labeled antibody as competitor with the antibody being detected (scheme 3 at top of col.3) therefore all components recited in claims 8-9 would have been obvious.

Claims 1-3, 5-7, 15 and 20-21 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Penfold et al (Graefe's archive for clinical and Exper. Opthalmol. Vol 228, 270, 1990—ref c77).

Penfold et al disclose detection of autoantibodies against retinal astrocytes in patients with age-related macular degeneration (AMD). In at least some samples, the autoantibodies appear to react with glial fibrillary acid protein; in any case, the detected autoantibody reactivity must reflect reactivity against some "macular degeneration associated molecule" since any antibody is reactive with an antigenic determinant on a molecule.

Penfold et al teach (page 274) that the presence of anti-astrocyte antibodies in the serum of patients with AMD "may form the basis of a diagnostic test." Thus the claimed invention would have been obvious; under anticipation, it is noted that Penfold shows everything recited after "comprising" and, thus,

merely "detecting" the autoantibody anticipates, irrespective of whether or not one is drawing any diagnostic inference from the autoantibody detection.

From the above claims 1, 3, 6 are anticipated or obvious.

Claim 2 is included because the examiner is not familiar with the nomenclature of the recited molecules; in the event that one of these is the same as what was designated as "glial fibrilary acid protein" of the reference then rejection is proper.

Claim 5 is rejected since there is a comparison with control sera.(page 270, col.2.)

Claim 15 is included, since the patients tested were examined by "opthalmologic procedures" (page 270, col.2).

Claims 20-21 are included since the glial fibrilary acid protein is a "retina-associated protein".

Claim 7 is included because Penfold et al's method forms a complex between autoantibody and antigen of a solid phase tissue section, prior to detecting the streptavidin-botin fluorescent labeling reagents. (page 271, col.1). Formation of an immune complex on a solid phase is deemed to be "precipitation" because applicant teaches solid phase capture of immune complexes with protein A or G and then teaches "the immunoprecipitates are washed" (page 15, last para.).

Claims 1, 3, 5-7, 15 and 20-21 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Gurne et al (ophthalmology, vol.98, 602,1991-ref 033).

Gurne et al detect autoantibodies against retinal proteins in the sera of proteins in the sera of patients with AMD. They employ western blotting or immunohistochemical methods to detect such autoantibodies.

Following the argument presented supra regarding Penfold et al, claims 1, 3, 6 and 20-21 are anticipated, since claim 1 merely requires detecting an autoantibody. If weight were given to diagnosing, then this would have been obvious because any chemical marker more prevalent in diseased than in control individuals can be employed for diagnosis.

Claim 5 is included since controls were studied (page 603, col.10).

Claim 15 is rejected since patients were diagnosed by "ophthalmic examination" (page 602, col.2).

Claim 7 is rejected because an immune complex of analye autoantibody and antigen is formed on the nitrocellulose solid phase, prior to detection with brotin avidin labeled reagents (page 603, col.2); as noted for Penfold et al, formation of an immune complex on a solid phase is deemed to be "precipitation."

Claims 1, 3, 5-7, 15 and 20-21 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Chen et al (Eye science, vol.9, 113, 1993—ref c6).

Chen et al teach detection of autoantibodies against retinal proteins in the serum of AMD patients. They teach detection via a western blotting method. They suggest use of such autoantibody detection for diagnosis/prognosis of the

disease (page 119, col.2). Following the rational stated supra for Penfold et al claims 1, 3, 6 and 20-21 are anticipated or obvious.

Claim 5 is rejected because Chen et al compare against controls (page 114, col.1).

Claim 15 is included since Chen et al conduct "ophthalmic examinations" (page 114, col.1).

Claim 7 is rejected because an immune complex of analyte autoantibody and antigen is formed on the nitrocellulose solid phase, prior to detection with biotin avidin labeled reagents (page 114, col.2); as noted regarding Penfold et al, formation of an immune complex on a solid phase is deemed to constitute "precipitation."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, PhD whose telephone number is 571-272-0849. The examiner can normally be reached on Monday-Thursday from 8:00a.m to 5:30 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information

for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Saunders/tgd

June 22, 2004

David A Saunders
DAVID SAUNDERS
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ART UNIT ~~182~~ 1644